What is the Role of Diffusion Weigh Magnetic Resonance Imaging in Evaluation of Thyroid Nodules?

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Abstract This study aimed to compare ultrasonography (US), contrast-enhanced computed tomography (CCT) of the neck, and diffusion-weight magnetic resonance imaging (DW-MRI) in differentiating between benign and malignant nodules while approaching to thyroid nodules, and to estimate sensitivity and specificity of these methods. On thyroid US, echogenicity, calcification, presence/absence of halo, nodule size being larger/smaller than 20 mm, and nodule nature (cystic/solid nature) were evaluated. Findings on CCT of the neck were grouped according to the heterogeneity/homogeneity, presence/absence of enhancement, and intensity. On DW-MRI, diffusion restriction was evaluated. The findings of these tests were compared with postoperative histopathological findings, and specificity and sensitivity of the tests in differentiating malignant and benign nodules were assessed. The study included 38 patients (34 females, 4 males). The sensitivity and specificity of DW-MRI were 20 and 75 %, respectively. Presence of a >20 mm nodule in thyroid US had the highest sensitivity, whereas thyroid fine-needle aspiration biopsy (FNAB) had the highest specificity in detecting

malignancy. The sensitivities and specificities of CCT of the neck and DW-MRI appeared relatively low. Evaluation of thyroid US findings together with thyroid FNAB findings provided high specificity and sensitivity and yielded better results than findings of CCT of the neck and DW-MRI.

Keywords Thyroid nodule · Diffusion-weight imaging · Neck tomography · Ultrasonography

Introduction

The incidence of thyroid nodules in the general population is between 4 and 7 % [1], of which 5–10 % have malignant character [2, 3]. Although there are numerous current approaches to evaluate thyroid nodules, a clear differentiation between malignant and benign nodules could not be achieved using none of these approaches.

Thyroid ultrasonography (US) is a quick, easily applicable and non-invasive technique that provides definite information about the size and nature of nodules. Thyroid US is quite successful in detecting millimetric nodules, which could not be palpated in the neck on physical examination. Thyroid US is usually the primary technique to be requested together with thyroid stimulating hormone measurement in a patient with detected or suspected thyroid nodule.

Biopsy via fine-needle aspiration, which has been widely used since early 1980s, has an important role in patient selection. Thyroid fine-needle aspiration biopsy (FNAB) is accepted as the most reliable diagnostic method for the differentiation of benign thyroid nodules from malignant thyroid nodules [1]. Since FNAB is a minimally invasive, cheap, reliable and well-tolerated method that

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rarely results in complications, it is the first choice to determine the character of thyroid nodules.

Although contrast-enhanced computed tomography (CCT) of the neck is not being routinely used to evaluate thyroid nodules, it is the method to determine the size of gland, whether the gland has retrosternal extension, and its relation with adjacent organs are in question.

Diffusion-weight magnetic resonance imaging (DW-MRI) is currently a first-choice method usually for ischemic cerebrovascular accidents (CVA); however, there is no information concerning its role in the evaluation of pathological characteristics of thyroid nodules.

The aim of the present study was to compare the results of thyroid US, CCT of the neck, thyroid FNAB and DW-MRI with histopathological findings and to estimate sensitivity and specificity of these methods.

Materials and Methods

Patients who were admitted to the Department of Ear Nose and Throat between 2009 and 2011 were included in the study. Those who previously underwent thyroid surgery due to either malignant or benign reason were excluded from the study. Surgical indication was determined based on the presence of compressive symptoms highly suggesting malignancy and on sonographic findings. Accordingly, hoarseness and difficulty in breathing were considered the compressive symptoms. Nodules larger than 20 mm and the presence of microcalcification were interpreted as suspicious sonographic findings for malignancy. A rapidly growing nodule was considered suspicious clinical finding for malignancy.

Surgery was decided directly in patients with suspicious or malignant FNAB results, whereas surgery was decided based on the clinical and sonographic findings in patients with biopsy report of inadequate specimen or benign lesion. Informed consents were obtained from the patients that would undergo surgical procedure. The patients also underwent CCT of the neck and DW-MRI in the supine position. Computed tomography was performed using Toshiba Activision TSX 031A (Toshiba Medical Systems Co., Tochigi-Ken, Japan). Iopamidol was used as the contrast agent; patients were administered 150 mL Iopamidol (300 mg/mL) via intravenous route through the antecubital region. DW-MRI was performed using the GE Signa HDxT 1.5 Tesla (GE Healthcare, Milwaukee, USA).

On US, nodule size, echogenicity, presence of calcification, presence of halo, and nature of the nodule were separately evaluated. Nodules larger than 20 mm were considered suspicious for malignancy. The echogenicity of the nodule was classified as hyperechogenic, hypoechogenic, isoechogenic or combined of all. The nature of the

nodule was evaluated in three groups as solid, cystic or mixed.

On CCT of the neck, presence of heterogeneity, presence of enhancement, and intensity (hyperintense, hypointense or normointense) were evaluated. On DW-MRI, diffusion restriction in the nodule was also evaluated.

Statistical Analysis

Statistical analysis was performed using the Number Cruncher Statistical System (NCSS) 2007 and the Power Analysis and Sample Size (PASS) 2008 Statistical Software program (Utah, USA). In addition to the descriptive statistics (mean, standard deviation, median, frequency, ratio), the Mann–Whitney *U* test was used for the comparison of the data. Qualitative data were compared using the Chi square and Fisher's Exact Chi square tests. Specificity, sensitivity, and positive and negative predictive values were calculated to evaluate the results of MRI, FNAB and US according to the pathology results. A *p* value <0.05 was considered statistically significant.

Results

The present study included 38 patients, of which 10.5 % (*n* = 4) were males and 89.5 % (*n* = 34) were females. The mean age of the patients was 46.81 ± 13.19 years (range 18–70 years).

There was no significant difference between the benign and malignant cases in terms of nodule natures (cystic, solid, and mixed) as determined on US (*p* > 0.05, Table 1).

According to the pathology results, malignancy was observed in 26.3 % of the cases and calcification was present in 34.2 % of the cases according to the US results. 6 (15.8 %) of 10 (26.3 %) cases, which were diagnosed with malignancy based on pathology, had calcification on US; since other cases were found to be normal, the sensitivity and specificity of the test were found to be 60.0 and 75.0 %, respectively. The positive and negative predictive

Table 1 Distribution of the nature of the nodules on ultrasonography (US) according to pathology results

	Pathology		<i>p</i>
	Benign (<i>n</i> = 28) <i>n</i> (%)	Malignant (<i>n</i> = 10) <i>n</i> (%)	
Nature			
Cystic	4 (14.3)	0 (0)	0.265
Solid	15 (53.6)	8 (80.0)	
Mixed	9 (32.1)	2 (20.0)	

Table 2 Evaluation of ultrasonographic calcification results according to the pathology results

US	Pathology		
	Malignant n (%)	Benign n (%)	Total n (%)
Calcification			
Present	6 (15.8)	7 (18.4)	13 (34.2)
Absent	4 (10.5)	21 (55.3)	25 (65.8)
Total	10 (26.3)	28 (73.7)	38 (100)
Sensitivity (%)		60.00	
Specificity (%)		75.00	
Positive predictive value		46.15	
Negative predictive value		84.00	

Table 3 Evaluation of enhancement on contrast-enhanced computed tomography (CCT) of the neck according to the pathology results

CCT of the neck	Pathology		
	Malignant n (%)	Benign n (%)	Total n (%)
Enhancement			
Present	1 (2.6)	4 (10.5)	5 (13.2)
Absent	9 (23.7)	24 (63.2)	33 (86.8)
Total	10 (26.3)	28 (73.7)	38 (100)
Sensitivity (%)		10.00	
Specificity (%)		85.71	
Positive predictive value		20.00	
Negative predictive value		72.73	

values of the test were 46.15 and 84.00 %, respectively (Table 2).

Only one (2.6 %) of 10 (26.3 %) cases, which were diagnosed with malignancy on pathology, showed enhancement on CCT of the neck; since the other cases were found to be normal, the sensitivity and specificity of the test were 10.0 and 85.71 %, respectively. The positive and negative predictive values of the test were 20.0 and 72.73 %, respectively (Table 3).

CCT of the neck revealed abnormal intensity in 36.8 % of the cases. CT revealed abnormal intensity in only one (2.6 %) of 10 (26.3 %) cases, which were diagnosed with malignancy based on pathology. Since other cases were normal, the sensitivity, specificity, positive predictive value, and negative predictive value of the test were 10.0, 53.57, 7.14, and 62.50 %, respectively (Table 4).

Evaluation of restriction on (DW-MRI) according to the pathology results are presented in Table 5.

Table 4 Evaluation of intensity on contrast-enhanced computed tomography (CCT) of the neck according to the pathology results

CCT of the neck	Pathology		
	Malignant n (%)	Benign n (%)	Total n (%)
Intensity			
Abnormal	1 (2.6)	13 (34.2)	14 (36.8)
Normal	9 (23.7)	15 (39.5)	24 (63.2)
Total	10 (26.3)	28 (73.7)	38 (100)
Sensitivity (%)		10.00	
Specificity (%)		53.57	
Positive predictive value		7.14	
Negative predictive value		62.50	

Table 5 Evaluation of restriction on diffusion-weight magnetic resonance imaging (DW-MRI) according to the pathology results

DW-MRI	Pathology		
	Malignant n (%)	Benign n (%)	Total n (%)
Restriction			
Absent	8 (21.1)	21 (55.3)	29 (76.3)
Present	2 (5.3)	7 (18.4)	9 (23.7)
Total	10 (26.3)	28 (73.7)	38 (100)
Sensitivity (%)		20.00	
Specificity (%)		75.00	
Positive predictive value		22.22	
Negative predictive value		72.41	

Discussion

On thyroid palpation, usually the nodules larger than 1 cm can be palpated. Occasionally, some experienced physicians can palpate the nodules smaller than 1 cm. Palpation of thyroid nodules may be problematic particularly in patients having a short and thick neck. Thus, imaging methods are frequently required [4, 5].

The first-line radiological method that should be used for the evaluation of thyroid nodules is thyroid US [6]. High-resolution thyroid US can easily detect nodules that are 1 mm or larger [7]. Although it is a subjective imaging method, thyroid US provides definite information on solid or cystic nature of the nodule, presence or absence of microcalcification, presence or absence of halo, and the size of nodule. In the present study, we evaluated the size and nature of the nodule and the presence of calcification separately in order to eliminate subjective interpretation related to US, and we avoided using a definite term or diagnosis such as benign or malignant based on the thyroid US findings. In the present study, the specificity of thyroid

US in detecting microcalcification, nodule nature and nodule size was found to be 75, 46 and 10 %, respectively. The sensitivity of thyroid US in detecting microcalcification, nodule nature and nodule size was 60, 80, and 80 %, respectively. In a similar US study conducted by Hasane-fendioğlu et al. [8], the specificity and sensitivity for microcalcification were reported to be 97 and 64 %, and the specificity and sensitivity for nodule nature were reported to be 48 and 94 %. When the results of the present study was compared with those of the above-mentioned study, the results were found similar; microcalcification appeared to be the most specific and nature appeared to be the most sensitive in favor of solid nodule. Pure cystic nodules are rare, and although they have low risk of malignancy, they are the candidates for thyroid FNAB [9, 10].

Although CCT of the neck is quite sensitive in detecting nodules, it fails to provide information about clinical behavior of the nodule. CCT of the neck is mostly used for large nodules with ill-defined borders, and it provides detailed information on adjacency [11].

CCT is superior to thyroid US in terms of showing presence or absence of invasion to the trachea, esophagus, vessel–nerve bundle, and infrahyoid muscles, presence of retrosternal extension, and adjacency in the superior mediastinum [12].

It should be kept in mind that, thyroid lymphomas do not invade infrahyoid muscle and vessel/nerve bundle, do not cause tracheal deviation, and do not show calcification on CCT of the neck [13].

In their study, Ishigaki et al. [14] compared multislice-computed tomography and thyroid US in 30 patients; they found thyroid US more valuable for the evaluation of thyroid nodules, reported the specificity of thyroid US in detecting malignant nodules to be 90 %, and concluded that diagnostic importance of thyroid US was superior to that of computed tomography.

In the present study, in differentiating malignant and benign nodules, the specificity of CCT of the neck for enhancement and intensity were found to be 85 and 53 %, respectively. According to the result of the present study, presence of enhancement on CCT of the neck is more specific than the calcification on thyroid US. In their study, Takashima et al. [15] reported that among the various sonographic signs, microcalcification showed a specificity of 93 % and a sensitivity of 36 %.

In their series of 31 patients, Tancredi et al. [16] evaluated the contrast enhancement rates of the nodules with suspicious thyroid FNAB findings on MRI according to their volumes, and compared them with histopathology results. Accordingly, the sensitivity and specificity were found to be 84 and 100 %, respectively, for nodules larger than 5 mm. The reason for such a high specificity might have resulted from performing the imaging in a selected

patient population (those with suspicious thyroid FNAB findings) and from the use of gadolinium as the contrast agent.

Thyroid FNAB is the minimal invasive method providing the most important information in determining the histopathological character of thyroid nodules. Some authors in the literature have defended that thyroid FNAB is the method that should be primarily used for the evaluation of nodules [10, 17, 18]. Although the number of unnecessary surgical procedures is reduced owing to the diagnostic role of thyroid FNAB in thyroid nodules, the incidence of carcinoma on histopathological evaluation of patients undergoing thyroidectomy has shown an increase [19, 20]. In their study, Amrikachi et al. [21] performed thyroid FNAB in 6,226 patients, and they reported sensitivity and specificity to be 93 and 96 %, respectively, for specimens considered adequate. In the present study, however, the sensitivity and specificity were found to be 30 and 96 %, respectively. We attributed such a difference in sensitivity to the large sample size and to the precondition of adequate diagnostic material during the selection of the slides. Disadvantages of thyroid FNAB include false negativity rates up to 30 % in the nodules larger than 3 cm and its partial subjectivity according to the pathologist that examines the specimen [22, 23]. In order to prevent this, it is recommended for the pathologist preferably to be a cytopathologist specialized in the field of thyroid diseases and we recommend a sampling by more than a single aspiration in the same session for the nodules larger than 3 cm.

Although thyroid FNAB is the gold standard for diagnosis, there are also suspicious or benign conditions which require surgery. Thus, certain clinical conditions should be considered while deciding for surgery; these conditions include age <20 or >45 years, male gender, presence of a nodule due to Graves' or Hashimoto's diseases, history of radiation to the head and neck region, family history of thyroid carcinoma, pain, signs of compression or invasion, cervical lymph node metastasis, thyroid nodules larger than 4 cm, rapid enlargement, and enlargement despite thyroid suppression therapy. Evaluation of these clinical criteria and sonopathological findings together with thyroid FNAB is the most effective approach to make a decision for surgical procedure or follow-up.

To the best of our knowledge, there is no information about the use of DW-MRI in approaching to thyroid nodules. In 2008, Razek et al. [24] investigated 30 patients to assess necrotic and alive parts of head and neck masses and detected severe diffusion restriction in the necrotic areas. In that particular study, it was concluded that biopsy should not be taken from the areas shining on DW-MRI in patients followed for malignancy. In our study, histopathology of two patients with diffusion restriction revealed partially

abscessed thyroid tissue, and this finding might be considered consistent with the above-mentioned study. In the present study, the sensitivity and specificity of DW-MRI in differentiating malignant and benign lesions were 20 and 75 % respectively; these ratios were low as compared with those of thyroid US and thyroid FNAB.

Conflict of interest None.

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